

Fig. 1

1/23

GLLPVLESFK VSFLSALEEY TKKLNTQ

Fig. 2a.1

HUMAN
Macaque
Bovine
Pig
Dog
Rabbit
Tree shrew
Mouse
Rat
Eur. Hedgehog
Chicken
Jap. quail
Domestic duck
Rainbow trout
Brown trout
Atl. salmon
Zebrafish
Sea bream

MKAAVLTTLAVLFLTGSQARHFQQDEPPQSPWDRVKDLATVYVDVLKDSGRDYSQFEQS
MKATVLTTLAVLFLTGSQARHFQQDEPPQTPWDRVKDLVTVYVEALKDSGKDYVSQFEQS
MKAVVLTTLAVLFLTGSQARHFQQDDP-QSSWDRVKDFATVYVEAIKDSGRDYVAQFEAS
MKAVVLTTLAVLFLTGSQARHFQQDDP-QSPWDRVKDFATVYVDVAIKDSGRDYVAQFEAS
MKAALLTLAVLFLTGSQARHFQQDEP-QSPWDRVKDLATVYVDVAIKDSGRDYVAQFEAS
MKAVVLTTLAVLFLTGSQARHFQORDEP-RSSWDKIKDFATVYVDTVKDSGREYVAQFEAS
MKAVVLTTLAVLFLTGSQARHFQQDEP-QSSWDRVRLANVYVDVAVKESGREYVSQLEAS
MKAVVLAVALVFLTGSQAWHVWQQDEP-QSQWDKVKDFANVYVDVAVKDSGRDYSQFESS
MKAVALAVALVFLTGCQAWFEWQQDEP-QSQWDRVKDFATVYVDVAVKDSGRDYSQFESS
-----DEA-KSYWDQIKDMLTVYVDATAKDSGKDYLTSLDTS
MRGVLVLTTLAVLFLTGTQARSFQWHDPE-QTPLDRIRDMVDVYLETVKASGKDAIAQFESS
MRGVLVLTTLAVLFLTGTQARSFQWHDPE-QTPLDRIRDMVDVYLETVKASGKDAIAQFESS
MRVVVLTALLFLTGTQARYFQWHDPE-QAPLDRRLDLVDVYLETVKASGKDAIAQFEAS
MKFLALALTILLAAQTQAFP-MQADAP--SQLEHVKAALSMYIAQVKLTAQRSIDLDDT
MKFLALALTILLAAATQAVP-MQADAP--SQLEHVKVAMMEYMAQVKETGQRSIDLDDT
MKFLVLTALLAAQTQAFP-MQADAP--SQLEHVKAALNMYIAQVKLTAQRSIDLDDT
MKFVALALTILLALGSQANL-FQADAP--TQLEHYKAAALVYLNQVKDQAEKALDNLDGT
MKFAALALALLLAVGSHAAS-MQADAP--SQLDHARAVLDVYLTQVKDMSLRVNLQDDP
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HUMAN
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Brown trout
Atl. salmon
Zebrafish
Sea bream

ALGKQLNLKLLDNWDSVTSTFSKLEQLGPVTQEFWDNLEKETEGLRQEMSKDLEEVKAK
ALGKQLNLKLLDNWDSVTSTVSKLEQLGPVTQEFWDNLEKETEGLRQEMSKDLEEVKAK
ALGKQLNLKLLDNWDTLASTLSKVREQLGPVTQEFWDNLEKETASLRQEMHKDLEEVKQK
ALGKHLNLKLLDNWDSLGSTFTKVREQLGPVTQEFWDNLEKETALRQEMSKDLEEVKKK
ALGKQLNLKLLDNWDSLSSTVTKLREQIGPVTQEFWDNLEKETEVLRQEMSKDLEEVKQK
AFGKQLNLKLLDNWDSLSSTVSKLQEQLGPTQEFWDNLEKETEGLRQEMSKDLEEVKQK
ALGKQLNLKLVNDWDTLGSTFQKVHEHLGPVAQEFWEKLEKETEEELRREINKDLEEVKQK
SLGQQLNLNLLNWDWDTLGSTVSQQLERLGPLTRDFWDNLEKETDWRQEMNKDLEEVKQK
TLGKQLNLNLLDNWDTLGSTVGRQLQEQLGPTQEFWANLEKETDWRNEMNKDLEENVKQK
ALGQQLNKKLADNWDVTSSALLKAREQMKPIAMEFWGNLEKDETEGLRQTVSKDLELVKEK
AVGKQLDLKLADNLDTLASAAAKLREDMAPYKEVREMWLKDTEALRAELTKDLEEVKEK
AVGKQLDLKLADNLDTLASAAAKLREDMAPYKEVREMWLKDTEALRAELTKDLEEVKEK
AVGKQLDLKLADNLDTLGAAAKLREDMAPYKEVREMWLKDTEALRAELTKDLEEVKEK
EY-KEYKMLTQSLDNLQYADATSSQLAPYSEAFGTQLTDATAAVRAEVMKDVEELRQ
EF-KEYKQLSLSLDNLQYQATTSQSLAPYSEAFGAQLTDAAAVRAEVMKDVEDVRTQ
EY-KEYKMLSLSLDNLQYFADSTSKSWPPTPRSS-APSCDATATVRAEVMKDVEDVRTQ
DY-EQYKLQSLSESLTKLQEYQATTSQALTPYAETISTQLMENKQLRERVMTDVEDLRSK
QY-AEFKTNLAQRIEEMYTQIKTLQGSVSPMTDSFYNTVMEVTKDTRSLNVDLEALKSS
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HUMAN
Macaque
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Tree shrew
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Chicken
Jap. quail
Domestic duck
Rainbow trout
Brown trout
Atl. salmon
Zebrafish
Sea bream

VQPYLDDFQKKWQEEEMELYRQKVEPLRAELQEGARQKLHELQEKLSPLGEEMRDRARAHV
VQPYLDDFQKKWQEEEMELYRQKVEPLRAELHEGTRQKLHELHEKLSPLGEEVRDRARAHV
VQPYLDEFQKKWHEEVEIYRQKVAPLGEEFREGARQKVQELQDKLSPLAQELRDRARAHV
VQPYLDDFQKKWQEEEMETYRQKMAPLGAEEFREGARQKVQELQEKLSPLAEELRDRARAHV
VQPYLDDFQKKWQEEVELYRQKVAPLGSELREGARQKLQELQEKLSPLAEELRDRARTHV
VQPYLDEFQKKWQEEEVERYRQKVEPLGAELRESARQKLTELQEKLSPLAEELRDRARTHV
TQPFLEIQQKWQEDLERYRQKVEPLSAQLREGARQKLMELQEQVTPLGEDLRDSVRAYA
VQPYLDEFQKKWKEDVELYRQKVAPLGAELQESARQKLQELQGRSLPVAEEFRDRMRTHV
MQPHLDEFQEKWNEEVEAYRQKLEPLGTELHKNA---KEMQRHLKVVAEEFRDRMRVNA
VQPYLDSFQKKVEEELLYRQKVAPLSAEWREARQKAQELQKAGELGQHRDRVRTHV
IRPFLDQFSKWTTEELEQYRQRLTPVAQELKELTKQKVELMQAKLTPVAEEARDRLRGHV
IRPFLDQFSKWTTEELEQYRQRLAPVAQELKDLTKQKVELMQAKLTPVAEEVRDRRLREQV
IRPFLDQFSKWTTEELEQYRQRLAPVAEELKELTKQKVELMQAKLTPVAEEARDRLRGHV
LEPKRAELKEVLDKHIDEYRKLEPLIKEHIELRRTEMAFRAKMEPIVEELRAKVAINV
LEPKRAELKEVLDKHIDEYRKLEPLIKEHIELRRTEMAFRAKMEPIVEELRAKVAINV
LEPKRAELTEVLNKHIDEYRKLEPLIKQHIELRRTEMAFRAKIDPVVEEMRAKVAINV
LEPHRAELYTALQKHIDEYREKLEPVFQEYSALNRQNAEQLRAKLEPLMDDIRKAFESNI
LAPQNEQLKQVIEKHLNDYRLLTPIYNDYKTKHDEEMAALKTRLEPVMEELRTKIQANV
* . : : : * : * : : * : : : *

09987107 11304

Fig. 2a.2

HUMAN	DALRTHLAPYSDELQRRLAARLEALKENGGARLAEYHAKATEHLSTLSEKAKPALEDLRQ
Macaque	DALRTHLAPYSDELQRRLAARLEALKENGGARLAEYHAKASEHLSTLSEKAKPALEDLRQ
Bovine	ETLRQQLAPYSDDLQRRLTARLEALKEGGG-SLAEYHAKASEQLKALGEKAKPVLEDLRQ
Pig	EALRQHVAPYSDDLQRMAARFEALKEGGG-SLAEYQAKAQEQLKALGEKAKPALEDLRQ
Dog	DALRAQLAPYSDDLRRERLAARLEALKEGGGASLAEYHARASEQLSALGEKAKPALEDLRQ
Rabbit	DTLRTKLAPYSNELQQRLLAARLESIKEGGGASLAEYQAKAREHLSVLSEKAKPALEDLRQ
Tree shrew	DTLRTQLAPYSEQMRKTLGARLEAIKEGGGASLAEYHAKASEQLSALGEKAKPVLEDIHQ
Mouse	DSLRTQLAPHSEQMRESLAQRLLAELKSNP--TLNEYHTRAKTHLKTGEKAKPALEDLRH
Rat	DALRAKFGLYSDQMRENLAQRLEIRNHP--TLIEYHTKAGDHLRTLGEKAKPALDDLQ
Eur. Hedgehog	DALRTDLAPYGEEARKLLQLRLQDIKAKSG-DLAEYQTKLSEHLKSFGEKAQPTLQDLRH
Chicken	EELRKNLAPYSDELQRKLSQKLEEIREEKGIPOASEYQAKVMEQLSNLREKMTPLVQEFRE
Jap. quail	EELRKNLAPYSSELQRKLSQKLEEIREEKGIPOASEYQAKVVEQLSNLREKMTPLVQEFKE
Domestic duck	EELRKNLAPYSDELQRKLSQKLEEIREEKGIPOAAEYQAKVVEQLSNLREKMTPLVQDFKE
Rainbow trout	EETKTKLMPIVEIVRAKLTERRLEELRTLAAPYAEYKEQMIKAVGEVREKVSPLSEDFKG
Brown trout	EETKTKLMPIVEIVRAKLTERRLEELRTLAAPYAEYKEQMFKAUGEVRKVGPLTNDFKG
Atl. salmon	EETKTKLMPIVEIVRAKLTERRLEELRTLAAPYAEYKEQMFKAUGEVRKVPALSEDFKA
Zebrafish	EETKSKVPMVEAVRTKLTERLEDLRTMAAPYAEYKEQLVKAVEEAREKIAPHTQDLQT
Sea bream	EETKAVLMPVETVRTKVTERLESREVVQPYVQYKEQMKQMYDQA-QTVD--TDALRT
	: : . . : : : : ** : : . . : :

HUMAN	GLLPVLESFKVSFLSALEEYTKKLNTQ
Macaque	GLLPVLESFKVSFLSALEEYTKKLSTQ
Bovine	GLLPVLESFKVSILAAIDEASKKLNAQ
Pig	GLLPVLENLKVSIILAAIDEASKKLNAQ
Dog	GLLPVLESFKVSLAAIDEATKKLNAQ
Rabbit	GLLPVLESFKASVQNVLDEATKKLNTQ
Tree shrew	GLMPMWESFKTGVNLVIDEAAKKLTA-
Mouse	SLMPMLETCLKTKAQSVIDKASETLTAQ
Rat	GLMPVLEAWKAKIMSMIDEAKKKLNA-
Eur. Hedgehog	GLEPLWEGIKAGAMSMLEELGKKLNSQ
Chicken	RLTPYAENLKNRLISFLDELQKSVA--
Jap. quail	RLTPYAENLKNRLIDLDELQKTMA--
Domestic duck	RLTPYAENLKTRFISLDELQKTVA--
Rainbow trout	QVGPAAEQAKQKLLAFYETISQAMKA-
Brown trout	QVGPAAEQAKEKLMDFYETISQAMKA-
Atl. salmon	RWAPPPRRPSK--SSWLSTRPSARP--
Zebrafish	RMEPYMENVRTTFAQMYETIAKAIQA-
Sea bream	KITPLVEEIKVKMNAIFEIIAASVTKS
	*

0987407 11301

sp	P06727	APA4	HUMAN
sp	P33621	APA4	MACFA
sp	P06728	APA4	MOUSE
sp	Q28758	APA4	PAPAN
sp	O46409	APA4	PIG
sp	P02651	APA4	RAT

sp	P06727	APA4_HUMAN
sp	P33621	APA4_MACFA
sp	P06728	APA4_MOUSE
sp	Q28758	APA4_PAPAN
sp	O46409	APA4_PIG
sp	P02651	APA4_RAT

sp	P06727	APA4_HUMAN
sp	P33621	APA4_MACFA
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sp	P33621	APA4_MACFA
sp	P06728	APA4_MOUSE
sp	Q28758	APA4_PAPAN
sp	O46409	APA4_PIG
sp	P02651	APA4_RAT

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QQEQVQMLAPLES 396
QQEQVQMLAPLES 429
-----PKPLES 395
QQEQVQMLAPLES 401
-----APLEG 382
-----PKPLES 391
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TOEFTT 20T28660

Fig. 3

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Exon 1 Exon 2

Trimer stabilising

Tripple alpha helical coiled coil
forming

E₁P₂P₂T Q K P K K I V N A K K D₁₆ V₁₇ V N T K M F E E L K S R L D T L A Q E V A L L K E Q Q A L Q T V C L₅₁

Fig. 4

6/23

Position	d	e	f	g	a	b	c	d	e	f	g	a	b	c	d	e	f	g	a	
Human tetranectin	V	V	N	T	K	M	F	E	E	L	K	S	R	L	D	T	L	A	Q	
Murine tetranectin	L	V	S	S	K	M	F	E	E	L	K	N	R	M	D	V	L	A	Q	
Bovine cart. protein	R	R	V	K	E	K	D	G	D	L	K	T	Q	V	E	K	L	W	R	
Shark cart. protein	S	K	S	G	K	G	K	D	D	L	R	N	E	I	D	K	L	W	R	
Consensus	L											h	y	L	E	V	L	K	E	
							</													

Fig. 6

pT7 H6UbiFx Cys-Apo A1

pBR328 - (PvuII) - GATCTCGATCCCGCGAAATTAATACGATACACTATAGGAGAGCCACAAACGGTTTCCCTCTAGAAATAATTTTGTAACTTT

T7 promoter

AAGAAGGAGATATACATATGGATCGCATCACCATCACCATGATCTTTGTGAAGACCCCTACTGGCAAAACCATCACCCCTTG

Nde I

E V E P S D T I E N V K A K I Q D K E G I P P D Q Q R L I F A
AGGTCGAGCCAGTGACACCATTTGAGAAATGTCAAAGCCAAATTCAGACAAAGGAGGTATCCACCTGACACGACGCGTCTGATATTTGCGG
G K Q L E D G R T L S D Y N I Q K E S T L H L V L R L R G G S
GCAACACGCTGGAAGATGGACGTACTTTGTCTGACTACAATATTCAAAAGGAGTCTACTTTCATCTTTGTGTGAGACITTCGTGGTGGATCCA

Bam HI

TCGAGGGTAGGGTGGATGTgatgaacccccccagagccccctgggagtcgagtgaaagacctggccactgtgtacgtggatgtgctcaaagacagcggcagagac
I E G R G G C D E P P Q S P W D R V K D L A T V Y V D V L K D S G R D
tatgtgtccagtttgaaggctccgcttgggaaacagctaaacctcttgacaaactgggacagcgtgacccctccaccttcagcaagctg
Y V S Q F E G S A L G K Q L N L K L L D N W D S V T S T F S K L
cgcaacacagctcgccctgtgacccagagttctgggataacctggaaaaggagacagagggcctgaggcagagatgagcaaggatctggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgaaggccaaaggtgcagccctacctggacgacttccagaagaagtggcaggaggatggagctctaccgcaagaaggtggagccgctgcgcga
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagctccaaagggcgccagaaagctgcacgagctgcaagagaagctgagccactgggcgaggagatgagcgacccgagcgccccatgtg
E L Q E G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgcgctgcgacgcatctggccccctacagcagcagctggcccgccgcttggccgagccttgaggctctcaaggagaaacggcgccgagaga
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggccgagtagtacacgccaaggccacgagcatctgagcacgctcagcgagaaggcccgccgctcgaggaacctccgccaaggccctgctgccc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgctggagagcttcaaggtcagcttccctgagcgctctcgagagtagtacactaagaagaagctcaacacccagTAAGCATGCAAGCTTGAATTCGATCC
V L E S F K V S F L S A L E E Y T K K L N T Q STOP SphI HindIII EcoRI

GGCTGTACAAAGCCCGAAAGGAGCTAGTTGGTGGCTGCCACCGCTGAGCTGAGCAATAACTAGCATAACCCCTCTG

CCACCGCTGTGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTTGTGAAGAGGAGGAATATATCCGAT - (EcoRV) - pBR328.

pT7H6 Trip-A-Apo A1 - Amp^R.

[illegible]

Fig. 8

pT7H6 Trip-A-Apo A1-del43 - Amp^R.

pBR328 - (PvuII) - GATCTCGATCCCGGAAATTAATACGATACACTATAGGAGACCAACAGGTTTCCCTCTAGAAATAATTTTGTAACTTTAAGAAAGGAGAT
T7 promoter
M G S H H H H H G S I Q G R S P G T E P P T Q K P K K I V N A K K
ATACATATGGGATCGCATCACCATCACCGATCGATCCAGGGTAGATCTCTGGTACCGAGCCCAACCCAGAGCCCAAGAGATTGTAAATGCCAAGAAA
Bgl II, Kpn I
D V V N T K M F E E L K S R L D T L A Q E V A L L K E Q Q A L Q T V S L
GATGTTGTGAACACAAAGATGTTTGAGGAGCTCAAGAGCCGCTCTGGACACCCCTGGCCAGGAGGTGGCCCTGTGTAAGGAGCAGCAGGCCCTGCAGACGGTCTCCCTG
Bam HI
AAGGATCCctaaagctccttgacaaactgggacacagcgtgacctccaccttcagcaagctg
K G S L K L L D N W D S V T S T F S K L
cgcgaaacagctcgccctgtgacccagaggagttctgtggataaacctggaaaaaggagacacagagggcctgagcgaggagatgagcaaggatctggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgaaggccaaaggtgcagccctacctggacgacttccagaagaagtggcaggaggagatggagctctaccgccagaaggtggagccgctgcgcgca
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagctccaaagagggcgccgagagctgcacgagctgcaagagaagctgagcccaactgggcgaggagatgcgcgaccgcgcgcgcgcctatgtg
E L Q E G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgctgcgcacgcatctgccccctacagcagcagctgcgcagcgttggccgcgccttgaggtctcaaggagaaacgcgccgagcaga
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggccgagtagtaccacgccaagggccaccgagcatctgagcacgctcagcgagaaggcccaagcccgctcgaggacctccgccaaggcctgctgccc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgctggagagcttcaaggctcagcttccctgagcgctctcgaggagtagctacactaagaagctcaacacccagTAATAAGCTTGAATTCGGATCCGGCTGCTAA
V L E S F K V S F L S A L E E Y T K K L N T Q STOP HindIII EcoRI
CAAAGCCCGAAAGGAAGCTGAGTTGGCTGCCTGCCACCGCTGAGCAATAACTAGCATAAACCCCTCTGCCACCGCTGTGGGGCCTCTAAACGGGTCTTTGAGGGG
TTTTTTGTGTAAGGAGGAACATATCCGAT - (EcoRV) - pBR328.

pBR328- (PvuII) -GATCTCGATCCCGCGAAATTAAACGATACACTATAGGAGACCAACGGTTTCCCTCTAGAAAATAATTTTGTGTTTAACTTTAAGAAGGAGATATA

T7 promoter

M G S H H H H H H G S I E G R

CATATGGGATCGCATCACCATCACCATCCGATCCATCGAGGGTAGG

Nde IBam HI

GGTGGATGTgatgaacccccccagagccctgggatcgagtgaggacctggccactgtgtactgtggatgtgtctcaaaagacagcgccagagac
G G C D E P P Q S P W D R V K D L A T V Y V D V L K D S G R D
tatatgtgtccagtttgaaaggtccgccttgggaaaaacagctaaaacctccttgacaaactgggacacgctgacctccaccttcagcaagctg
Y V S Q Q F E G S A L G K Q L N L K L L D N W D S V T S T F S K L
cgcgaacagctcggccctgtgacccagagttctgggataacctggaaaaaggagacagagggcctgaggcaggagatgagcaaggatctcggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgtaaggcccaaggtgcagccctacctggaagacttccagaagaagtggcaggaggagatggagctctaccgccagaaaggtggagccgctgcgcgca
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagctccaagagggcgcgccagaaagctgcacgagctgcaagagaagctgagccactggcgaggagatgcgacccgcgcgcgccatgtg
E L Q E G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgcgctgcgcacgcatctggccctacagcgacgagctgcgcagcgcttggccgcgccttgaggctctcaaggagaacggcgcgccaga
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggcggagtaccacgccaagggccacgagcatctgagcagctcagcgagaaggccaagccgcgctcgaggacctccgcaaggcctgctgccc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgtgtagagcttcaaggtcagcttctctgagcgctctcagggagtacactaagaagctcaacacccagTAAGCATGTCAAGCTTGAATTCGGATCC
V L E S F K V S F L S A L E E Y T K K L N T Q STOP Sphi HindIII EcoRI

GGCTGCTAACAAAGCCGAAAGGAGCTGAGTTGGCTGGCTGCCACCGCTGAGCTGAGCAATAACTAGCATAAACCCCTCTG

CCACCGCTGTGGGCCCTCTAAACGGGCTCTTGAGGGGTTTTTTGCTGAAGGAGGACTATATCCGAT-(EcoRV)-pBR328.

Fig. 10a

pT7H6 Trip-A-Apo A1 K9A K15A - Amp^R.

pBR328 - (PvuII) - GATCTCGATCCCGGAAATTAAATACGATACACTATAGGAGAGACCACACGGTTTCCCTCTAGAATAAATTTTGTAACTTTAAGAAGGAGAT
T7 promoter
M G S H H H H H G S I Q G R S P G T E P P T Q K P K A I V N A K A
ATACATATGGGATCGCATCACCATCACCATCAGGATCGATCCAGGTAGATCTCTGTATCCGAGCCACCAACCCAGAGCCCAAGGCGATTGTAAATGCCAAGGCA
D V V N T K M F E E L K S R L D T L A Q E V A L L K E Q Q A L Q T V S L
GATGTTGTGAACACAAAGATGTTGAGGAGCTCAAGAGCCGCTCTGGACACCCCTGGCCAGGAGGTGGCCCTGCTGAAGGAGCAGCAGGCCCTGCAGACGGTCTCCCTG
Bam HI
AAGGATCCGATGATGAAACCCCGAGAGCCCTGGGATCGAGTGAAGGACCTGGCCACTGTGTACTGTGATGTGCTCAAAAGACAGCGGCAGAGAC
K G S D E P P Q S P W D R R V K D L A T V Y V D V L K D S G R D
tatgtgtccagttgaaggctccgcttgggaaacacagctaaacctaagctccttgacaaactgggacagctggacgtgacctccaccttcagcaagctg
Y V S Q F E G S A L G K Q L N L K L L D N W D S V T S T F S K L
cgcaaacagctcgccctgtgacccaggttctgtggataacctggaaaaaggagacagagggccctgagggcaggagatgagcaaggatctggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgaaggccaagggtcagccctacctggacgacttccagaagaagtggcaggagagatggagctctaccgccagaaaggtggagcgcgtgcgcgca
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagctccaagagggcgccagaaagctgcacgagctgcaagagaagctgagccactgggagggagatgagcgacccgagcgccgccccatgtg
E L Q E G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgcgtgcgcacgcatctggccccctacagcgacgagctgcgccagcgttggccgagcgttggaggtctctcaaggagaaacggcgccagaga
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggccgagtaccacgccaaggccacgacatctgagcacgctcagcgagaaggccaagcccgctcgaggacacctccgccaaggcctgtgcccc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgctggagagcttcaaggctcctgagcgtctctcgaggagtacactaagaagctcaacacccagTAATAAGCTTGAATTCGATCCGGCTGCTAA
V L E S F K V S F L S A L E E Y T K K L N T Q STOP HindIII EcoRI
CAAAGCCGAAAGGAAGCTGAGTTGGCTGCCACCGCTGAGCTGAGCAATAACTAGCATAAACCCCTCTGCCACCGCTGTGGGCGCTCTAAACGGGTCTTGAGGGG
TTTTTTTGTGAAAGGAGGAACTATATCCGAT - (EcoRV) - pBR328.

pT7H6 Trip-A-Fn-Apo A1 - Amp^R.

Fig. 10b

pBR328- (PvuII) - GATCTCGATCCCGGAAATTAATACGATACACTATAGGAGACCACAACGGTTTCCCTCTAGAAATAATTTTGTAACTTTAAGAGGAGAT
T7 promoter
M G S H H H H H G S G S I Q G R S P G T E P P T Q K P K I V N A
ATACATATGGGATCGCATCACCATCACCATCAGGATAGGTAGTGATCAATCCAGGGTAGATCTCCTGGTACCGAGCCACCACCCAGAAGCCCAAGAAGATTGTAATGCC
Bgl II Kpn I
K K D V V N T K M F E E L K S R L D T L A Q E V A L L K E Q Q A L Q T V S L
aAGAAAGATGTTGTGAACACAAAGATGTTTGAGGAGCTCAAGAGCCGCTCTGGACACCCCTGGCCAGGAGGTGGCCCTCTGCTGAAGGAGCAGCAGGCCCTGCAGACGGTCTCCCTG
Bam HI
AAGGATCCTcgggtcatgatgaacccccccagagccccctgggacgcagtgaaggacctggccactgtgtacgtggatgtgtctcaaaagacagcggcagagac
K G S s g h D E P P Q S P W D R V K D L A T V Y V D V L K D S G R D
tatgtgtcccgatttgaaggctccgcttgggaaacacagctaaacctaagctccttgacaaactgggacagcgtgacctccaccttcagcaagctg
Y V S Q F E G S A L G K Q L N L K L L D N W D S V T S T F S K L
cgcgaacagctcggccctgtgacccaggagttctgggataacctggaaaaggagacagagggccctgagggcaggagatgagcaaggatctggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgaaggccaaggtgcagccctacctggacgacttccagaagaagtggcaggaggagatggagctctaccgcccagaaggtggagccgctgcgcgca
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagctccaagagggcgccagagctgcacgagctgcaagagaagctgagccactgggagaggagatgcgcgaccgcgcgccccatgtg
E L Q E G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgcgtgcgcacgcatctggccccctacagcagcagctgcgcagcgttggccgcgcccttgaggtctcctcaaggagaaacggcgccaga
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggccgagttaccacgccaaggccacgagcatctgagcagctcagcagaaggcccgccgctcgaggacctccgccaaggcctgtgccc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgctggagagcttcaaggtcagcttctcagcgtctctcagaggtagtacactaagaagctcaacacccagTAATAAGCTTGAATTCGATCCGGCTGCTAA
V L E S F K V S F L S A L E E Y T K K L N T Q STOP HindIII EcoRI
CAAGCCCGAAGGAAGCTGAGTTGGCTGCCCTGCTGAGCTGAGCAATAACTAGCATACCCCTCTGCCACCGCTGTGGGGCTCTAAACGGGTCTTGAGGGG
TTTTTTGCTGAAGGAGGAACACTATATCCGAT- (EcoRV) -pBR328.

pT7H6 Trip-A-Fn-Apo A1 final K9AK15A - Amp^R.

Fig. 10d

pBR328- (PvuII) -GATCTCGATCCCGGAATTAATACGATACACTATAGGGAGACCACACCGTTTCCCTCTAGAAATAATTTTGTTAACTTTAAGAAGGAGAT
T7 promoter
M G S H H H H H G S G S I Q G R S P G T E P P T Q K P K A I V N A
ATACATATGGGATCGCATCACCATCACCGTAGTGTAAGGATCAATCCAGGGTAGATCTCTCTGTACCGAGCCACCAACCCAGAGCCCAAGCGGATTGTAAATGCC
Bgl II Kpn I
K A D V V N T K M F E E L K S R L D T L A Q E V A L L K E Q Q A L Q T V S L
AAGGCAGATGTTGTGAACACAAAGATGTTTGAGGAGCTCAAGAGCCGTCTGGACACCTGGCCAGGAGGTGGCCCTGTCTGAAGGAGCAGCAGGCCCTGCAGACGGTCTCCCTG
Bam HI
AAGGGAACCTcgggtcaggatgaacccccccagagccccctgggagtcgagtgaggacctggccactgtgtacgtggatgtgctcaagacagcggcagagac
K G T s g q D E P P Q S P W D R V K D L A T V Y V D V L K D S G R D
tatgtgtccagttgaaggctccgccttgggaaacagctaaacctaaagctccttgacaaactgggacagcgtgacctccaccttcagcaagctg
Y V S Q F E G S A L G K Q L N L K L D N W D S V T S T F S K L
cgcaaacagctcggccctgtgacccagaggttctgggataaacctggaaaaggagacagaggccctgaggcaggagatgagcaaggatctggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgaaggccaaaggtgcagccctacctggacgacttccagaagaagtggcaggagagatggagctctaccgccagaaggtggagccgctgcgcgca
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagctccaagagggcgccgagagctgcacgagctgcaagagaagctgagccactgggcgaggagatgcgcgaccgcgcgcgccccatgtg
E L Q E G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgcgctgcgcacgcatctggccccctacagcgacgagctgcgccagcgttgccgcgccttgaggctctcaaggagaaacggcgccagaga
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggccgagtagtaccacgccaaggccacggagcatctgagcacgctcagcgagaaggcccaagccgcgctcgaggacacctccgccaaggcctgctgccc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgctggagagcttcaaggtcagcttccctgagcgctctcgaggagtagactaagaagctcaacacccagTAATAAGCTTGAATTCGGATCCGGCTGCTAA
V L E S F K V S F L S A L E E Y T K K L N T Q STOP HindIII EcoRI
CAAAGCCGAAAGGAAGTGAGTTGGCTGCCACCGCTGAGTGAGCAATAACTAGCATAACCCCTCTGCCACCGCTGTGGGGCCTCTAAACGGGTCTTGAGGGG
TTTTTTGCTGAAAGGAGGAACATATATCCGAT- (EcoRV) -pBR328.

Fig. 10e

pT7H6 (GS) 3 Trip-A-Tn-Apo A1 Amp^R.

pBR328- (PvuII) -GATCTCGATCCCGGAAATTAATACGATACACTATAGGAGACCACAACGGTTTCCCTCTAGAAATAAATTTTGTAACTTTAAGAGGAGAT
T7 promoter
M G S H H H H H H H G S G S I Q G R S P G T E P P T Q K P K K I V N A
ATACATATGGGATCGCATCACCATCACCATCGGTAGTGGTAGTCAATCCAGGGTAGATCTCCTGGTACCGAGCCACCACCCAGAAAGCCCAAGAGATTGTTAAATGCC
Bgl II Kpn I
K K D V V N T K M F E E L K S R L D T L A Q E V A L L K E Q Q A L Q T V S L
aGAAAGATGTTGTGAACACAAAGATGTTTGGAGAGCTCAAGAGCCGTCTGGACACCCTGGCCAGAGGTTGGCCCTGCTGAAGGAGCAGCAGGCCCTGCAGACGGTCTCCCTG
Bam HI
AAGGATCCCAAGGTGCACATGAAGgaacccccccagagccccctgggatcagtgaaaggacctggccactgtgtacgtggatgtgtcctcaagacagcggc
K G S K V H M K D E P P Q S P W D R V K D L A T V Y V D V L K D S G
agagactatgtgtccagttgaaggctccgcttgggaaacagtaaacctaaagctccttgacaaactgggacagcgtgacctccaccttcagcaagctg
R D Y V S Q F E G S A L G K Q L N L K L L D N W D S V T S T F S K L
cgcaacagctcggccctgtgacccagagttcttgggataaacctggaaaggagacagagggcctgagcgaggagatgagcaaggatctggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgaaggccaaggtgcagccctacctggacgacttccagaagaagtggcaggaggagatggagctctaccgccagaaggtggagcgtgcgcgca
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagtccaagagggcgccagaaagctgcacgagctgcaagagaagctgagccactggcgaggagatgctgcgacccgcgccgccccatgtg
E L Q E G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgcgtgcgacgcatctggccccctacagcagcagctgcgcccagcgttggccgcgcccttgaggctctcaaggagaacggcgccaga
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggccgagtagtaccacgcaaggccacgagcatgtgacacgctcagcagagaaggccaagcccgctcagggacctccgcaaggcctgctgccc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgtggagagcttcaaggtcagcttccctgagcgtctcagggagtagtacactaagaagctcaacacccagTAATAAGCTTGAATTCGGATCCGGCTGTAA
V L E S F K V S F L S A L E E Y T K K L N T Q STOP HindIII EcoRI
CAAGCCGAAAGGAAGCTGAGTTGGCTGCCACCGCTGAGCTGAGCAATAACTAGCATAACCCCTCTGCCACCGCTGTGGGGCCTCTAAACGGGTCTTGAGGGG
TTTTTTGCTGAAAGGAGGAATATCCGAT- (BcorV) -pBR328.

pr7H6 Trip-A-Tn-Apo A1-final - Amp^R.

Fig. 10f

pBR328- (PvuII) - GATCTCGATCCCGGAAATTAATACGATACACTATAGGAGACCAACAGGTTTCCCTCTAGAAATAATTTGTGTTTAACTTTAAAGAAGGAGAT
T7 promoter
M G S H H H H H H H G S G S G S I Q G R S P G T E P P T Q K P K K I V N A
ATACATATGGGATCGCATCACCATCACCATCAGGTAGTGGTAGTGGATCAATCCAGGGTAGATCTCCTGGTACCGAGCCACCACCAAGAGGATTTGTAATGCC
Bgl II Kpn I
K K D V V N T K M F E E L K S R L D T L A Q E V A L L K E Q Q A L Q T V S L
aAGAAAGATGTTGTGAACACAAAGATGTTTGAGGAGCTCAAGAGCGCTTGACACCCCTGGCCAGGAGGTGGCCCTGTGAAGGAGCAGCAGGCCCTGCAGACGGTCTCCCTG
Bam HI
AAGGAACCAAGGTGCACATGAAGgaacccccccagagccccctgggacgcagtgaggacactggccactgtgtacgtggtgtgtcctcaagacagcggc
K G T K V H M K D E P P Q S P W D R V K D L A T V Y V D V L K D S G
agagactatgtgtcccagtttgaaggctccgcttggaacacagctaaacctaagctccttgacaaactgggacagcgtgacctccaccttcagcaagctg
R D Y V S Q F E G S A L G K Q L N L K L L D N W D S V T S T F S K L
cgcgaacagctcggccctgtgacccagggagttctgggataacctggaaaaggagacagagggccctgaggcaggagatgagcaaggatctggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgaaggccaaaggtgcagccctacctggacgacttccagaagaagtggcaggaggagatggagctctaccgcccaagaaggtggagccgctgcgcga
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagctccaagagggcgccagaaagctgcacgagctgcaagagaagctgagccccactggcgaggagatgcgcgacccgcgcgccccatgtg
E L Q E G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgcgtgcgcacgcacatctggccccctacagcgacgagctgcgccagcgttgcccgccgcttgaggctctcaaggagaacggcgccagaga
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggccgagtagtaccacgcaaggccacgagcatctgagcacgctcagcgagaaggcccaagcccgctcgaggacctccgccaaggcctgctgccc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgctggagagcttcaaggtcagcttctgagcgctctcgaggagtagacactaagaagctcaacacccagTAATAAGCTTGAATTCGCATCCGGGTGCTAA
V L E S F K V S F L S A L E E Y T K K L N T Q STOP HindIII EcoRI
CAAAGCCGAAAGGAAGTGAAGTGGCTGCCTGCCACCGCTGAGCTGAGCAATAACTAGCATAACCCCTCTGCCACCGCTGTGGGGCTCTAAACGGGTCTTGAGGGG
TTTTTTGCTGAAAGGAGGAACATATCCGAT- (EcoRV) -pBR328.

ptT7H6 Trip-A-Tn-Apo A1 final K9AK15A-Amp^R.

pBR328 - (PvuII) - GATCTCGATCCCGCGAAATTAAATACGATACATATAGGAGACCAACAACGGTTTCCCTCTAGAAATAAATTTGTTTAACTTTAAGAAAGGAGAT

T7 promoter

M G S H H H H H G S G S I Q G R S P G T E P P T Q K P K A I V N A
ATAATATGGGATCGCATCACCATCACCATCAGGTAGTGGTAGTGGATCAATCCAGGGTAGATCTCTGGTACCGAGCCACCAACCCAGAAGCCCAAGCGGATGTAAATGCC
K A D V V N T K M F E E L K S R L D T L A Q E V A L L K E Q Q A L Q T V S L
AAGGCAGATGTTGTGAACACAAAGATGTTTGAGGAGCTCAAGAGCCGTCTGGACACCCCTGGCCCAAGAGGTGGCCCTGCTGAAGGAGCAGCAGGCCCTGCAGACGGTCTCCCTG
Bam HI
AAGGGAACCAAGGTGCACATGAAGGAacccccccagagccccctgggatacgagtgaaggacctggccactgtgtacgtggatgtgtctcaaaagacagcggc
K G T K V H M K D E P P Q S P W D R V K D L A T V Y V D V L K D S G

agagactatgtgtcccgatttgaaggctcgccttgggaaacacagctaaccctaaagctccttgacaactgggacacgctgacctccaccttcagcaagctg
R D Y V S Q F E G S A L G K Q L N L K L L D N W D S V T S T F S K L
cgcgaacagctcggccctgtgacccagaggttctggataacctggaaaaggagacagagggcctgagcgaggagatgagcaaggatctggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgaaggccaaggtgcagccctacctggacgacttccagaagaagtggcaggaggagatggagctctaccgccagaagggtggagccgtgcgcgca
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagctccaagagggcgccagaaagtgcacgagctgcaagagaagctgagccactggcgaggagatgcgcgaccgcgcgcgcccatgtg
E L Q E G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgcgtgcgcagcatctggccccctacagcgacgagctgcgccagcgttggccgcgccttgaggtctcctcaaggagaacggcgccgca
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggcggagtaccacgccaaggccaccgagcatctgagcagctcagcgagaagcccgccgcgtcgaggtcctcgcccaaggcctgtgc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgtggagagcttcaaggctcctgagcgtctctcgaggagtacactaagaagctcaacacccagTAATAAGTTGAATTCGATCCGGCTGCTAA
V L E S F K V S F L S A L E E Y T K K L N T Q STOP HindIII EcoRI
CAAAGCCCGAAAGGAGCTGAGTTGGCTGCTGCCACCGTGAGTGAAGCAATAACTAGCATAACCCCTCTGCCACCGCTGTGGGGCCTCTAAACACGGGTCTTGAGGGG
TTTTTGTCTGAAAGGGAACATAATCCGAT- (EcoRV) - pBR328.

pT7H6 Hp-alpha-Apo A1 - Amp^R.

pBR328 - (PvuII) - GATCTCGATCCCGCGAAATTAATACCATACACTATAGGAGAGCACCAACGGTTTCCCTCTAGAAAATAATTTGTTTAACTTTAAGAAGGAGAT

T7 promoter

M G S H H H H H G S I Q G R G V D S G N D V T D I A D D G C P K P P E
ATAATATAGGATCGCATCACCATCACGGATCCAGGTTAGAGTGTGGactcaggcaatgatgtcacggatcgcatgacggctgccgaagccccccgag
attgcacatggctatgtggagcactcggttcgtaccagttaagaactactacaaactgcacagaaggagatggagtatacaccttaaacatgagaagcag
I A H G Y V E H S V R Y Q C K N Y Y K L R T E G D G V Y T L N N E K Q
tgataaataaaggctgttgagataaaacttcctgaatgtgaagcagtagctgggaagcccaagaatccggcaaacccagtgacagATCC
W I N K A V G D K L P E C E A V A G K P K N P A N P V Q R S
gatgaacccccagagccccctgggatcgagtgaaggacctggccactgtgtactgtgtctcaaaagacacagcggcagagac
D E P P Q S P W D R V K D L A T V Y V D V L K D S G R D
tatgtgtccagtttgaaggctccgccttgggaaaaacagctaaaccttcttgacaaactgggacagcgtgacctccaccttcagcaagctg
Y V S Q F E G S A L G K Q L N L K L L D N W D S V T S T F S K L
cgcgaacagctcggccctgtgacccaggaagtcttggtataacctggaaaaaggagacagagggcctgagcagaggagatgagcaaggatctggaggag
R E Q L G P V T Q E F W D N L E K E T E G L R Q E M S K D L E E
gtgaaggccaaggtgcagccctacctggacgacttccagaagaagtggcagaggagatggagctctaccgccagaaggtggagccgctgcgcgca
V K A K V Q P Y L D D F Q K K W Q E E M E L Y R Q K V E P L R A
gagctccaaggcgcgcgcagagaagctgcacgagctgcaagagaagctgagccccactgggcgaggagatgcgcgaccgcgcgcgccatgtg
E L Q E G G A R Q K L H E L Q E K L S P L G E E M R D R A R A H V
gacgcgtgcgcacgcacatctggccccctacagcgacgagctgcgccagcgttggccgcgccttgaggtctctcaaggagaacggcgcgcgcaga
D A L R T H L A P Y S D E L R Q R L A A R L E A L K E N G G A R
ctggccgagtaccacgccaaggccacgagcatctgagcacgctcagcgagaaggcccaagcccgctcgaggacctccgccaaggcctgctgccc
L A E Y H A K A T E H L S T L S E K A K P A L E D L R Q G L L P
gtgctggagagcttcaaggctcagcttcctgagcgcctctcgaggagtagactaagaagctcaacacccagTAATAAGCTTGAATTCGATCCGGCTGCTAA
V L E S F K V S F L S A L E E Y T K K L N T Q STOP HindIII EcoRI

CAAAAGCCGAAAGGAAGCTGAGTTGGCTGCGTCCACCGCTGAGCTAGCAATAAAGCTAGCTATTAACCCCTCTGCGCACCGCTGTGGGGCCCTCTAAACGGGTCTTTGAGGGG
TTTTTTTGCTAAAGGAGGAATATATCCGAT - (EcoRV) - pBR328.

Fig. 11

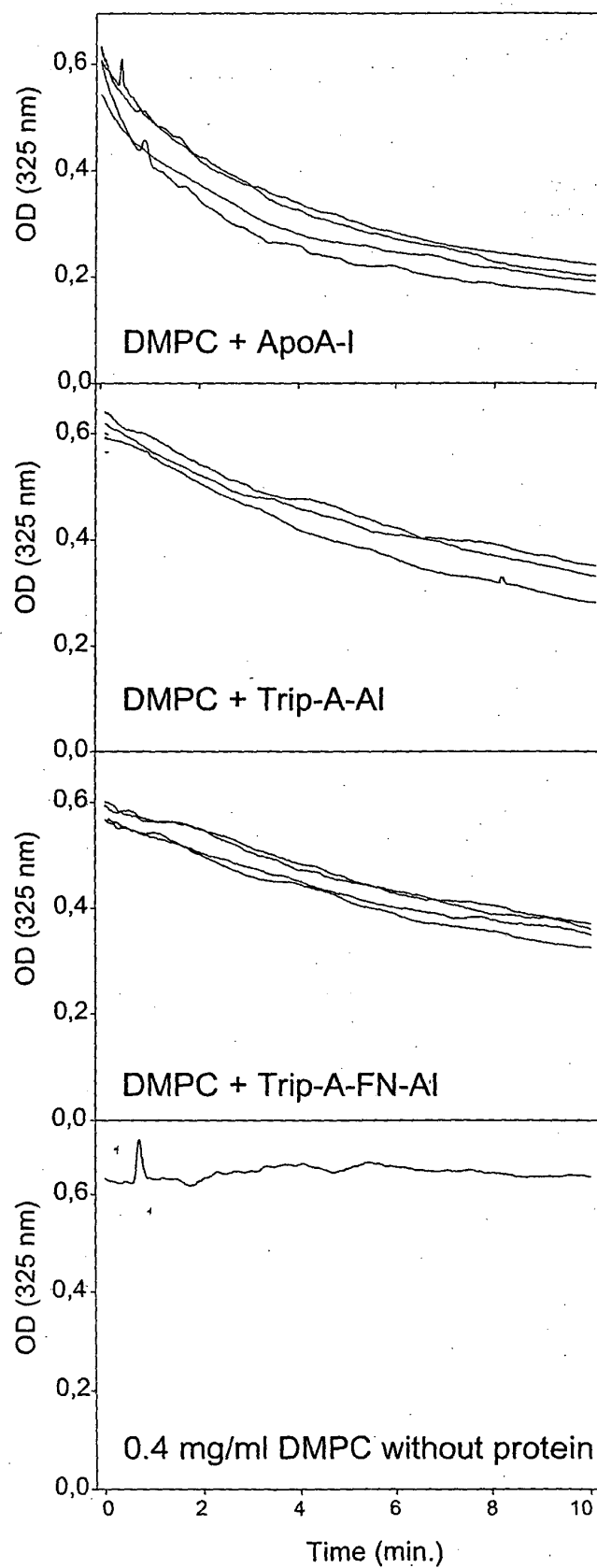


Fig. 12

Binding of apo A-I and Trip-A-I to immobilised cubilin

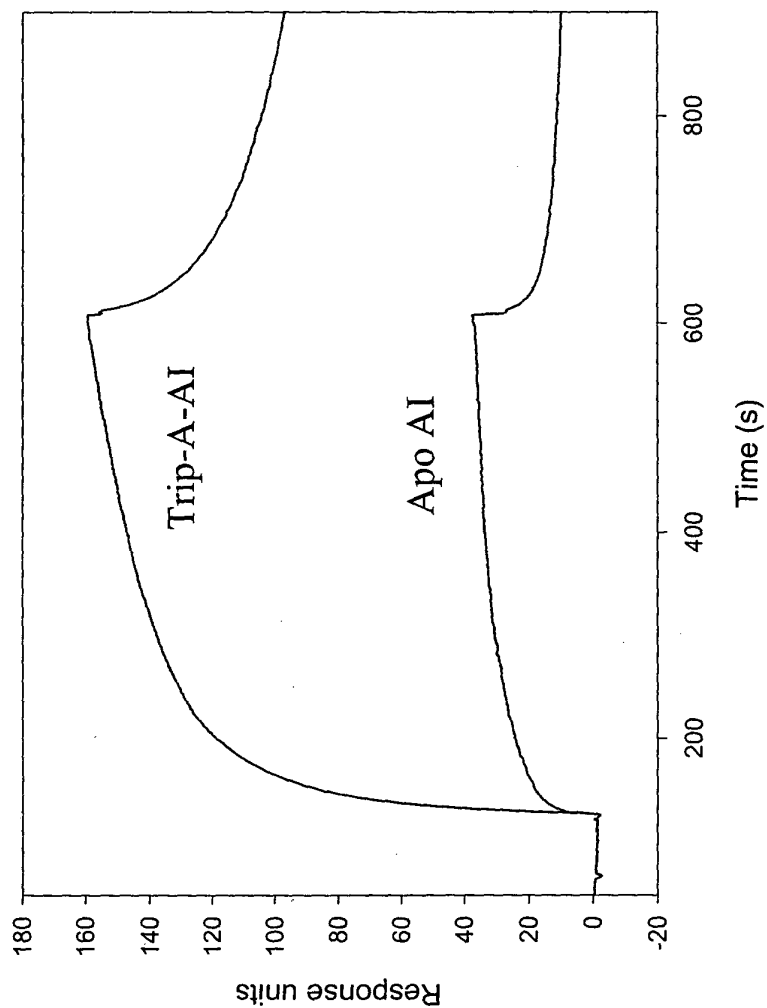


Fig. 13

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Superdex 200 analysis of apolipoprotein A-I derivatives

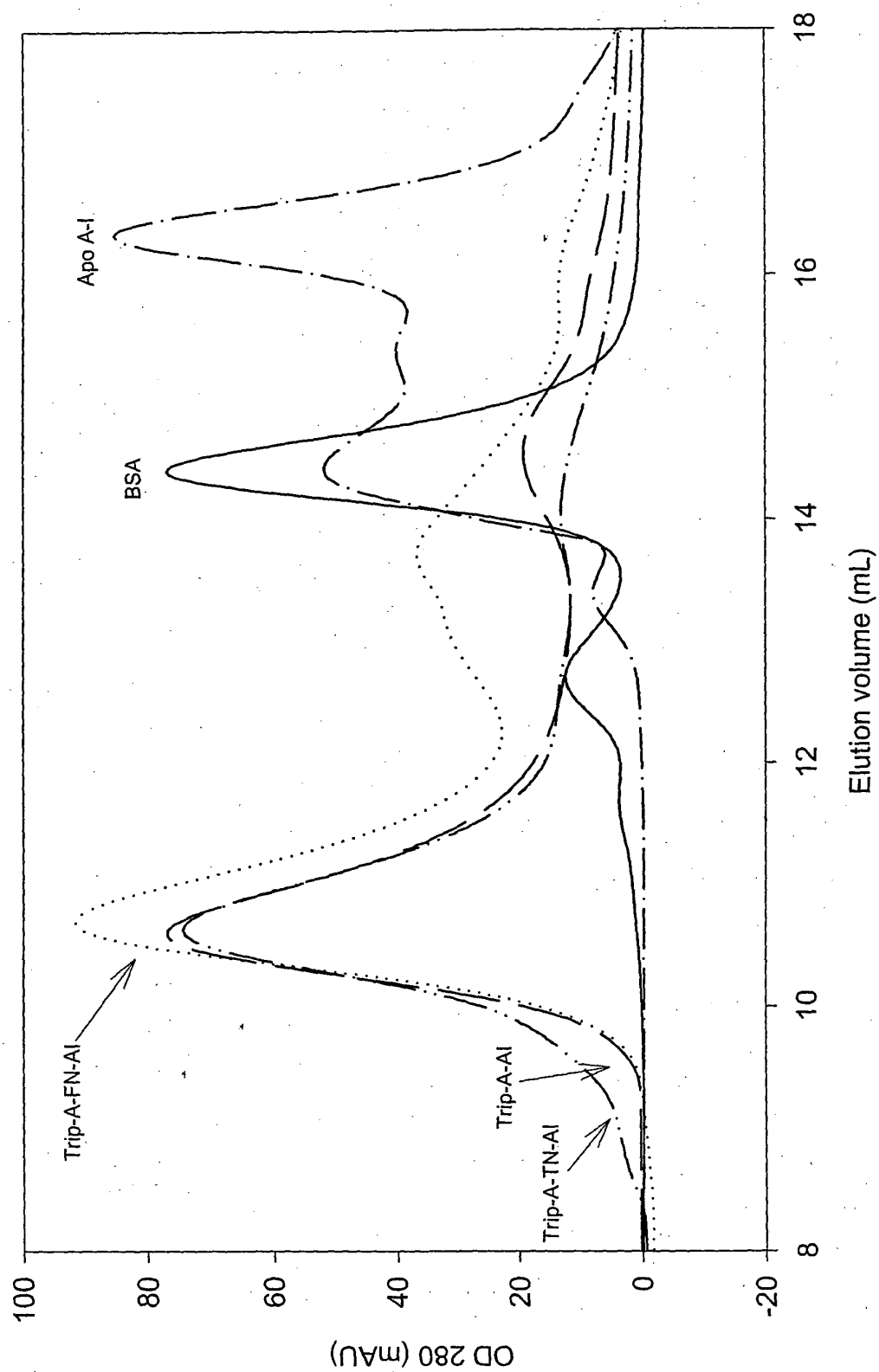
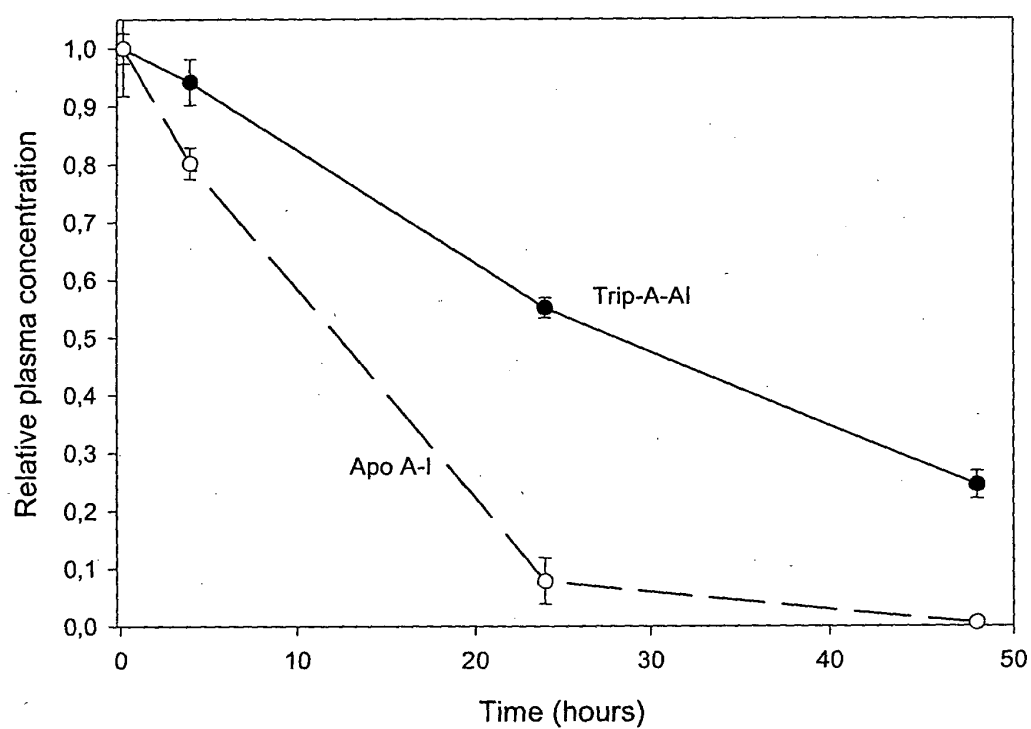


Fig. 14

Comparison of the plasma concentration of
Trip-A-A-I and Apo A-I over a 2 days period after
injection of 1 mg, mean of five mice



TOFTT-2018660